

## **REMARKS**

### **I. Status of the application**

Claims 3 and 20 – 42 are pending in the application, with claims 3 and 36-38 withdrawn from consideration. Claims 20-35 and 39-42 stand rejected. Claim 20 has been amended and support for such amendment can be found throughout the specification, drawings, and claims as originally filed.

### **II. Claim 20 is definite**

Claim 20 stands rejected under 35 U.S.C 112, second paragraph as being indefinite. This rejection is respectfully traversed.

The Examiner states that the limitation “the isoelectric point” in line 1 and “the pH” in line 4 lack antecedent basis. The term “the isoelectric point” does have antecedent basis. The claims are drawn to, “A method of determining the isoelectric point of a charged analyte.” Further, an isoelectric point is an inherent property of an analyte.

Similarly, the term, “the pH” inherently has antecedent basis. Claim 20 requires “changing the pH of the flowing liquid.” There is antecedent basis for “the flowing liquid,” so there inherently is antecedent basis for “the pH of the flowing liquid.” Liquids have a pH, so the term “the pH of the flowing liquid” has antecedent basis. Further, reciting “changing a pH of the flowing liquid” could be misunderstood to imply there is more than one pH. The present claim language avoids that possible confusion.

### **III. Claims 20, 22, 27-32, and 39-42 are patentable over Wu, Ivory, and Luner**

Claims 20, 22, 27 – 32, and 39-42 stand rejected under 35 U.S.C. 103(a) over Wu et al. (Capillary isoelectric focusing with a Universal Concentration Gradient Imaging System Using a Charge-Coupled Photodiode Array, Anal. Chem. 1992, 64, 2934-41) in view of Ivory et al. (U.S. Patent No. 6,277,258) as evidence by Luner et al (U.S. Pat No. 3,664,939). This rejection is respectfully traversed.

The references, alone or in combination, fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data.

Wu fails to teach or suggest changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, as required by independent claim 20. The Examiner refers to page 2939, column 2, lines 1-2 of Wu to teach changing the pH of the flowing liquid. These lines do not discuss changing the pH of the flowing liquid, but simply refer to “carrier ampholytes of pH 3-10.” Wu does not teach changing the pH of the flowing liquid, only that different pH carrier ampholytes may be used.

Wu in fact, teaches away from changing the pH of the flowing liquid. At page 2934, column 1, Wu describes conventional CIEF, which uses a subsequent mobilization process by adding salt to one of the capillary ends, resulting in a pH shift. Wu then goes on to say that, “[t]he performance of CIEF can be greatly improved in these aspects by *eliminating the mobilization process*.” (page 2934 column 2 first full paragraph) (emphasis added). Wu teaches away from changing the pH of the flowing liquid because of distortion of the linear pH gradient, difficulty of determining the pH values, and the long time required for mobilization (page 2934, column 2, lines 1-15). Based on these teachings, the skilled artisan, guided by Wu, would not change the pH of the flowing liquid, as required by independent claim 20.

Ivory fails to cure the deficiency of Wu. Similar to Wu, Ivory teaches an electrophoretic method for focusing a charged solute (Column 3 lines 14-16). Ivory does not teach changing the pH of the flowing liquid. In order to reach the subject claim limitations, the Examiner has relied on Ivory as a sample preparation method, assuming that the skilled artisan would change the pH of the flowing liquid in between sample preparation and determining the isoelectric point. However, the Examiner has not cited any reference or set forth any reasoning as why the skilled artisan would essentially repeat the focusing step other than to say, “because the step allows

concentrating the sample from a diluted sample prior to separation which would enhance separation.” (Office Action page 4). That falls short of teaching the claim limitation.

In any event, the combination of references relied on does not result in the claimed invention. Claim 20 requires determining the pH of the flowing liquid and the corresponding position of the focused band of the charged analyte at a plurality of band positions within the electric field gradient; and determining the isoelectric point of the charged analyte based on the multiple pHs and corresponding position data. If Ivory were used as a sample preparation method, followed by Wu’s method of determining the isoelectric point, the position data would not include a plurality of band positions, as required by independent claim 20. The isoelectric point would be determined based on only one position, not a plurality of band positions.

Luner also fails to cure the deficiency of Wu. Luner merely discloses that the pH of the focused ampholyte may be used to determine the isoelectric point of the same ampholyte. See col. 1, lines 29-33 of Luner. Each reference fails to teach or suggest determining an isoelectric point for a charged analyte by utilizing pH and corresponding position data of the charged analyte, at a plurality of positions, in an electric field gradient.

The references, alone or in combination, fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data.

**IV. Claims 21, 24, 26, 33, and 35 are patentable over Wu, Ivory, and Luner in further view of Yang**

Claims 21, 24, 26, 33, and 35 stand rejected under 35 U.S.C. 103(a) over Wu, Ivory, and Luner, and further in view of Yang et al (U.S. Pat. No. 4,666,855). This rejection is respectfully traversed.

As previously discussed Wu, Ivory, and Luner fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Yang fails to cure the deficiencies of Wu, Ivory, and Luner. Applicant requests that the rejection be reconsidered and withdrawn.

**V. Claim 23 is patentable over Wu, Ivory, and Luner, and further in view of Malabarba**

Claim 23 stands rejected under 35 U.S.C. 103(a) over Wu, Ivory, and Luner, and further in view of Malabarba et al (U.S. Pat. No. 5,521,155). This rejection is respectfully traversed.

As previously discussed Wu, Ivory, and Luner fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Malabarba fails to cure the deficiencies of Wu, Ivory, and Luner. Applicant requests that the rejection be reconsidered and withdrawn.

**VI. Claim 25 is patentable over Wu, Ivory, and Luner, and further in view of Zhu**

Claim 25 stands rejected under 35 U.S.C. 103(a) over Wu, Ivory, and Luner, and further in view of Zhu et al (U.S. Pat. No. 5,110,434). This rejection is respectfully traversed.

As previously discussed Wu, Ivory, and Luner fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Zhu fails to cure the deficiencies of Wu, Ivory, and Luner. Applicant requests that the rejection be reconsidered and withdrawn.

**VII. Claim 34 is patentable over Mazzeo, Luner, Witt and further in view of Ness**

Claim 34 stands rejected under 35 U.S.C. 103(a) over Wu, Ivory, and Luner, and further in view of Ness et al (U.S. Pat. No. 6,613,508). This rejection is respectfully traversed.

As previously discussed Wu, Ivory, and Luner fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient to form a focused band at a first stable position, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte to a second stable position, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Ness fails to cure the deficiencies of Wu, Ivory, and Luner. Applicant requests that the rejection be reconsidered and withdrawn.

### VIII. Conclusion

Applicant requests that the amendments presented above be entered in the patent application, and that the application be reconsidered. Applicant submits that all claims pending in the application are now in condition for allowance.

A petition for a one-month extension of time under 37 C.F.R. 1.136(a) and the accompanying fee are filed herewith. The Commissioner is hereby authorized to charge any such fees or credit any overpayment of fees to Deposit Account No. 19-0733.

Respectfully submitted,

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